REMARKS

Claims 31-62 are currently pending in the application. Claims 31-38, 42, 44, 48-50 and 52-60 have been withdrawn from consideration. New claims 63-67 are being added to the application in this amendment, and incorporate one of the alternatives of the claimed invention as set forth in claim 39, and therefore do not contain new matter.

In the Office Action, the Examiner has acknowledged the previously submitted amendments to claims 39-41, 43, 45-47, and 51; the addition of claims 61-62; and the amendment to the Abstract. The Examiner has acknowledged the claim for foreign priority under 35 U.S.C. § 119(a)-(d) and receipt of the certified copies of the priority documents. The Examiner has acknowledged receipt of the Information Disclosure Statement and the references cited therein. The drawings have been approved. Finally, the Examiner has withdrawn the rejection of claims 39-41 under 35 U.S.C. § 102(e) for anticipation by United States Patent No. 5,801,037 to Behnke et al.

In the Office Action, the Examiner has rejected claims 39-41, 43, 45-47, 61 and 62 for various reasons, and has objected to claims 43, 51, and 61-62 for various reasons. The Examiner continues to indicate that claim 51 is allowable, but stands objected to because claim 51 depends on rejected claim 47.

Claim Objection

The Examiner has objected to claims 43 and 61-62 for informalities. Claim 43 has been amended by deleting the portion of the claim that was directed to non-elected inventions. Claims 61 and 62 have been amended to recite properly a Markush group. Applicant believes that the amendments submitted herewith overcome the objections to claims 43 and 61-62.

35 U.S.C. § 112 Rejections

The Examiner has rejected claims 39-41 and the claims that depend thereon (claims 43, 45-47, 51, 61-62) under 35 U.S.C. § 112, second paragraph, for indefiniteness as set forth in paragraphs 8-12 on pages 3-6 of the Office Action.

The Examiner has rejected claims 39-41 as set forth in paragraph 8 of the Office Action by asserting that the recitation of "derivative having essentially the amino acid sequence as depicted in Figure 1 (SEQ ID NO: 1)" is indefinite because the phrase "having essentially the amino acid sequence" is a relative term for which a meaning is not provided in the specification. Claim 39 has been amended to recite a "staphylokinase derivative comprising an amino acid sequence which differs from SEQ ID NO: 1 due to substitution of at least one amino acid therein . . .." This recitation defines the nature of the staphylokinase derivative as having the amino acid sequence of SEQ ID NO: 1 having at least one amino acid substituted therein. Additionally, claims 40 and 41 have been amended by deleting the asserted indefinite language and depending on the definite recitation of "The staphylokinase derivative as claimed in claim 39, . . ." with a further limitation of the invention as claimed.

The Examiner has rejected claim 39 as set forth in paragraph 9 of the Office Action by asserting that the recitation "amino acid sequence as depicted in figure 1 (SEQ ID NO: 1) reactivity with panel of . . ." is unclear in meaning. Claim 39 has been amended to recite " . . . staphylokinase derivative has a reduced reactivity with a panel . . ." meaning that the reactivity of monoclonal antibodies raised for staphylokinase specific activity have a reduced reactivity with the staphylokinase derivative as claimed.

The Examiner has rejected claims 46-47 as set forth in paragraph 10 of the Office Action by asserting that the recitation of known amino acid substitutions at specific

positions of SEQ ID NO: 1 is unclear. Claim 39, as amended, now recites that the staphylokinase derivative has a sequence that is different than SEQ ID NO: 1 due to amino acid substitutions. Claim 45 recites a polyethylene glycol coupling to the cysteine substituted in SEQ ID NO: 1. Claim 46, as amended, recites a specific region at the amino-terminal end of SEQ ID NO: 1 where cysteine is substituted. Claim 47, as amended, recites specific positions at the amino-terminal end of a staphylokinase derivative having SEQ ID NO: 1 where the cysteine substitution takes place.

The Examiner has rejected claim 61 as set forth in paragraph 11 of the Office Action by asserting that the meaning of "amino acid substituted with Cys is at least one of a surface exposed residue" is unclear. Claim 61 has been amended to recite a Markush group for the amino acid residue that is substituted with cysteine.

The Examiner has rejected claim 62 as set forth in paragraph 12 of the Office Action by asserting that the recitation "amino acid substituted with Cys is the position of the polyethylene glycol coupling" is unclear. Claim 62 has been amended to recite "a polyethylene glycol is coupled to the substituted cysteine" in order to define clearly this claim limitation.

The Examiner has rejected claims 39-41, 43, 45-47 under 35 U.S.C. § 112, first paragraph, as set forth in paragraphs 13 through 15 of the Office Action by asserting that the amended claims contained new matter. The Examiner asserts that the previous amendment to include the phrase "the binding epitope and the activation epitope" is not supported in the specification and is therefore impermissible new matter. In addition, the Examiner asserts that the previous amendment to claim 61 that adds the limitation that the amino acid substituted is a "surface-exposed residue" is not supported in the specification.

Claim 39 has been amended to remove the phrase "the binding epitope and the activation epitope" in order to overcome the rejection.

The Examiner has rejected claims 39-41, 43, 45-47, 61-62 as set forth in paragraph 16-19 by asserting that the claims contain matter that was not described in the specification to convey to one skilled in the art that the inventors at the time of filing the application had possession of the invention. On page 7, paragraph 16 of the Office Action, the Examiner asserts that the specification fails to disclose (1) other staphylokinases as encompassed by the claims from organisms other than *S. aureus*; (2) the binding epitope or the activation epitope in any staphylokinase; (3) which amino acid residues can be substituted with Cys in any staphylokinase and still retain at least 50% of the specific activity of the corresponding wild-type staphylokinase; and (4) which are the surface exposed residues in a staphylokinase and which of these surface exposed residues can be substituted without losing activity. Moreover, the Examiner states that the specification discloses only a few species of the genus, which is assertedly insufficient to put one of ordinary skill in the art in possession of all attributes and features of all the species within the genus.

Claims 39-41, 43, 45-47, 61-62, as amended herewith and in accord with the disclosure of the specification, reasonably convey to one skilled in the relevant art that the inventor at the time of filing the application had possession of the invention. The arguments set forth by the Examiner in aforementioned points (1) through (4) are now moot in view of the claim amendments submitted herewith. Claim 39, as amended, clearly defines the nature of the staphylokinase derivative as having been cysteine-substituted. Certain claims have been amended to remove the asserted "new matter" even though the "binding epitope" and "activation epitope" of staphylokinase derivatives are known in the art. Certain dependent

claims, as amended, particularly recite which amino acids of SEQ ID NO: 1 must be substituted in order to obtain 50% specific activity of wild-type staphylokinase. Claim 63 requires both amino acid substitution and pegylation

The Examiner has rejected claims 39-41, 43, 45-47, 61-62 as set forth in paragraph 20-23 of the Office Action by asserting that the specification, while being enabling for the staphylokinase variant labeled SY19 (S3C-MP5), does not enable any person skilled in the art to make and use the invention commensurate in scope with the claims. In paragraph 20 on page 10 of the Office Action, the Examiner asserts that the scope of the claims is not commensurate with the enablement provided in regard to the extremely large number of unknown staphylokinases encompassed by the claims.

Claims 39-41, 43, 45-47, and 61-62, as amended, clearly define the scope of the claimed staphylokinase derivative as having an amino acid that differs from SEQ ID NO: 1 due to substitution of amino acids therein with another amino acid, namely, cysteine. Claims 40-41, 43, 45-47, and 61-62 include limitations that further define the location on the staphylokinase derivative and specific position of the amino acid sequence where the amino acid substitutions take place. Claim 63 requires both amino acid substitution and pegylation, and the claims which depend from claim 63 mirror certain claims which depend from claim 39. The claims, as amended, contain limitations that provide sufficient guidance that precludes undue experimentation for the preferred embodiments of the invention.

Obviousness-type Double Patenting Rejection

The Examiner has rejected claims 39-41, 43, 45, 61-62 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 3-5 of United States Patent No. 6,383,483 to Collen (hereinafter "the Collen patent"). In

addition, the Examiner has rejected provisionally claims 39-41, 43, 45, and 61-62 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 7-8 of co-pending United States Patent Application No. 09/728,670. United States Patent No. 6,383,483 and United States Patent Application No. 09/728,670 are being assigned to Désiré José Collen and Thromb-X N.V., the record title owners of this application. These assignments will be recorded in due course to establish that the cited patent and patent application are commonly owned with this application. Thereafter, a proper terminal disclaimer in compliance with 37 C.F.R. § 1.321(c) will be filed in due course in connection with this application in order to overcome the double-patenting rejection.

In view of the above amendments and remarks, it is believed that the claims are in condition for allowance. Reconsideration of the rejections is requested. Allowance of claims 39-41, 43, 45-47, 51, and 61-67 is respectfully requested.

Respectfully submitted,

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